EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCIATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCIATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, v. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES, Defendants.	Civil Action No. 1:23-cv-00707

BRIEF OF THE BIOSIMILARS FORUM
AS *AMICUS CURIAE* IN SUPPORT OF PLAINTIFFS'
MOTION FOR SUMMARY JUDGMENT

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Statutes & Regulations

Other Authorities

INTRODUCTION AND INTEREST OF *AMICUS CURIAE*

The Biosimilars Forum (the "Forum") is an independent, nonprofit trade association dedicated to advancing biosimilar medicines in the United States. As explained in more detail below, biosimilars are analogous to generic drugs in that they rely on FDA's safety and efficacy determinations for previously approved biological products. Like generic drugs, biosimilars can expand access to high-quality treatment options for patients suffering from a wide variety of conditions, including cancer, kidney disease, diabetes, and arthritis. The members of the Biosimilars Forum are the companies with the most significant U.S. biosimilar portfolios, including both biosimilars currently on the market and those still in development. Forum members were among the first companies to develop and launch biosimilars in the United States, and they continue to be the companies with the most knowledge and experience in this important industry.[1]

As a result, the Forum is familiar with the high cost and regulatory challenges associated with developing biosimilars and bringing them to market—with the consequent need for regulatory clarity and certainty in this complex area. The Forum is therefore well positioned to explain to this Court the adverse consequences of the Inflation Reduction Act ("IRA") on the biosimilars industry—and the millions of patients who stand to benefit from improved access to critical medicines thanks to biosimilars—reflecting the IRA's unconstitutional delegation of unchecked regulatory power and its denial of basic protections required by due process.

[1] For a complete list of members, *see* https://biosimilarsforum.org/about-us/members.

ARGUMENT

The IRA violates the separation of powers and due process guaranteed by the U.S. Constitution. It strips away multiple layers of constitutional protections designed to ensure political accountability and protect constitutional government, simultaneously delegating sweeping powers to the Secretary of Health and Human Services—who has in turn delegated that discretion to the Centers for Medicare and Medicaid Services ("CMS")—and insulating key agency decisions from public input and administrative or judicial review.

While these aspects of the IRA are problematic across the board, their potential impact on the biosimilars industry throws the broader constitutional problems with the statute into high relief. Congress intended competition from biosimilars to reduce prices of biological products through market competition rather than regulatory fiat. But the IRA's opaque and unconstitutional price-control scheme threatens to chill biosimilar development and decrease competition. To make matters worse, CMS—relying on the IRA's grant of discretion to initially implement the statute through purportedly unreviewable "guidance"—has adopted numerous positions that have no basis in the statute and that will be damaging to biosimilar development. These harmful consequences flow from, and confirm, the constitutional violations at the heart of the IRA, and they underscore why this Court should grant plaintiffs' motion for summary judgment.

I. Congress intended biosimilars to bring down prices of biological products through competition rather than top-down regulation.

Biological products are complex medicines that "are usually made from living sources such as proteins, living cells, and microorganisms such as bacteria or yeast."[2] *See* 42 U.S.C. § 262(i)(1) (defining "biological product"). Before such products can be introduced into interstate commerce,

[2] FDA, Are You on a Biologic Medication? at 1, *available at* https://www.fda.gov/media/165656/download (last accessed Aug. 24, 2023).

they must be licensed by FDA. 42 U.S.C. § 262(a)(1). Biological products play a critical role in the treatment of many serious illnesses, ranging from cancers to gastrointestinal diseases to genetic disorders, but they are often complex to develop and manufacture. The benefits of biological products thus come at a cost: Although biological products represent only 2% of all U.S. prescriptions, they account for nearly 40% of net drug spending in the United States.[3]

To reduce cost and increase patient access to these important medicines, Congress in 2010 enacted the Biologics Price Competition and Innovation Act ("BPCIA"). *See* Pub. L. No. 111-148, §§ 7001-7003, 124 Stat. 119, 804-21 (2010). The BPCIA created an abbreviated pathway for bringing to market "biosimilar" versions of already-licensed biological products. In order for a biosimilar to be approved and licensed, the manufacturer must show that it is "highly similar" to the previously licensed biological product—known as the "reference product"—and that there are "no clinically meaningful differences" between the two in terms of "safety, purity, and potency." 42 U.S.C. § 262(i)(2), (k)(2)(A)(i)(I). To balance competition with innovation, the BPCIA also provides a 12-year exclusivity period during which FDA's approval of a biosimilar cannot be made effective. 42 U.S.C. § 262(k)(7)(A).

Biosimilars provide meaningful, lower-cost alternatives for patients. In so doing, they help bring down the price of reference biological products too—not through top-down price controls, but through free-market competition. FDA approved the first biosimilar less than 10 years ago. Since then, biosimilars have generated substantial savings and improved patient access to critical medications. On average, the sales price of reference biological products that are competing with biosimilars has fallen 25%. *See* Ass'n for Accessible Meds., The U.S. Generic & Biosimilar

[3] *See* Biosimilars Forum, Saving Billions on Healthcare Costs with Biosimilars, https://biosimilarsforum.org/wp-content/uploads/Biosimilars-Saving_Healthcare_Costs.pdf.

Medicines Savings Report at 24 (Sept. 2022).[4] Biosimilars produced more than $13 billion in savings from 2015 through 2021, including $7 billion in 2021 alone. *Id.* at 23. They have been used in over 364 million days of patient therapy, including over 150 million additional days of therapy that otherwise would not have been provided. *Id.* at 22. The use of new biosimilars has saved patients with cancer more than $3.5 billion and cut the growth rate in oncology spending by nearly half. *Id.* at 26. In short, biosimilars play a vital role in helping patients afford treatment to manage life-threatening and chronic conditions, and robust competition between biosimilars and their reference products leads to lower prices across the board.

Biosimilars provide significant benefits to patients and the healthcare system, but developing a biosimilar and bringing it to market is expensive and time consuming. The process begins with candidate selection and refinement; many candidates considered for biosimilarity do not make it past early development thresholds. Those that do must then run a gauntlet of stringent analytical and clinical testing. The biosimilar manufacturer must also establish and scale up its commercial manufacturing process and pass rigorous FDA inspections. Once a biosimilar licensing application is submitted, FDA typically will take at least a full year to review and take action on the application.[5] All told, biosimilar development typically takes up to nine years and costs up to $300 million.[6] It is thus difficult for biosimilar manufacturers to make the investments

[4] *Available at* https://accessiblemeds.org/sites/default/files/2022-09/AAM-2022-Generic-Biosimilar-Medicines-Savings-Report.pdf.

[5] *See* FDA, Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027, *available at* https://www.fda.gov/media/152279/download.

[6] *See* Miriam Fontanillo et al., McKinsey & Co., *Three imperatives for R&D in biosimilars* (Aug. 19, 2022), https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars.

necessary to bring a new biosimilar to market without a predictable regulatory environment to provide some certainty that they will be able to recover their investment.

II. The IRA's unconstitutional delegation of price-control authority will chill biosimilar development.

The IRA casts a shadow that threatens to upset the balance struck by the BPCIA and impede the development of biosimilars, to the detriment of patients and the entire U.S. healthcare system. And it does so through an unprecedented scheme of price controls that violates the separation of powers and due process protections.

Price-setting regimes must be approached carefully, lest they intrude on private rights and undermine the public interest in maintaining the flow of goods and services. Wielded incautiously, the power to set prices may result in devastating consequences, such as causing drug shortages or undermining patient access. To mitigate these consequences, the Constitution requires Congress to provide appropriate standards, ensure public comment and proper rulemaking, and establish guardrails against administrative overreach. Congress has occasionally imposed price-setting regimes in other contexts, and when it has done so, it has abided by these fundamental constitutional principles. Here, however, Congress sought to sidestep these constitutional requirements and avoid political accountability by disguising its price-control regime as a "negotiation" while delegating to CMS virtually unfettered discretion to impose confiscatory prices by administrative fiat, without the crucial checks provided by meaningful statutory standards, public input, and administrative and judicial review. And that price-fixing fiat is backed by the threat of extraordinarily harsh penalties.

Operating through this novel and unconstitutional scheme, the IRA threatens to squeeze out competition from biosimilars. When a product is selected for price controls under the IRA, the statute requires CMS to reduce the product's price by *at least* 25 to 60 percent, *see* 42 U.S.C.

§ 1320f-3(b)(2)(F), (c), and it does not impose any investment-protecting floor or other meaningful constraints—not even a requirement (as in other price-control statutes) that prices be "just and reasonable." The scheme instead simply directs CMS to achieve the lowest possible price. *Id.* § 1320f-3(b)(1). As plaintiffs' motion explains, this standardless delegation violates the separation of powers. It also threatens to severely curtail the market-based price check provided by biosimilars. If CMS imposes no-floor price controls on a reference biological product, it will frequently be difficult, if not impossible, for a biosimilar to compete with that biological product on price and still be able to recoup its investment. Manufacturers thus may forgo making significant investments, and some may exit the biosimilars industry altogether. This will mean fewer low-cost drugs will be available for *all* patients—not only those enrolled in the federal healthcare programs where the IRA's price controls apply, but also those with private insurance and those who pay out of pocket. The IRA's chilling effect on biosimilar development will also increase the likelihood of damaging drug shortages in the event that a reference product manufacturer experiences supply disruptions, as there will be no biosimilar to fill the gap.

Congress recognized this reality, so it included provisions in the IRA that are intended to preserve biosimilar competition. To that end, biological products that are subject to competition from a licensed biosimilar are expressly exempt from price controls under the IRA. For example, the IRA states that a biological product is not subject to price "negotiation" in the first place if it is the reference product for a "licensed and marketed" biosimilar. 42 U.S.C. § 1320f-1(e)(1)(B). And if price controls are imposed on a biological product, those controls must be lifted once a biosimilar version of that product is licensed and "marketed pursuant to such … licensure." *Id.* § 1320f-1(c)(1). In addition, under a provision known as the "Biosimilar Special Rule," the Secretary can delay imposing price controls on a biological product for up to two years if the

biosimilar manufacturer requests such delay and shows a "high likelihood" that within that two-year period the biosimilar "will be licensed and marketed." *Id.* § 1320f-1(f)(1)(A).

But while these provisions seek to preserve some of the incentives for biosimilar development that existed before the IRA, they do nothing to cure the unconstitutional delegation at the heart of the IRA's price-control scheme, as they provide no guidance whatsoever to guide and constrain CMS's price-setting decisions and facilitate judicial review of those decisions. Nor do these provisions eliminate the IRA's chilling effect on biosimilars. Biosimilar development decisions must be made many years in advance: As noted above, the process of developing a biosimilar can take up to 9 years, and FDA cannot approve the biosimilar until 12 years after first licensure of its reference product. The IRA's price-control regime means that all of that investment must take place under the cloud of the risk that CMS may choose the biosimilar's reference product for price controls before the biosimilar is even eligible for approval and well after the manufacturer has invested time and resources to develop the biosimilar. And the IRA's unconstitutional delegation scheme, implemented through agency guidance without appropriate public input and shielded from judicial review in violation of the separation of powers and due process, means that Congress may be able to avoid political accountability for the choices CMS makes and their potentially devastating consequences for patients and the healthcare system.

Even for biosimilars that are near application submission or have been licensed, Congress provided no mechanism for a biosimilar manufacturer to be able to predict whether the reference product will be selected for price controls. Nor did CMS endeavor to help, stating instead in its Guidance that it does not intend to provide any advance notice of, or seek any public input regarding, the likelihood that a given biological product may be selected, or even to identify and disclose the specific data it intends to use. CMS states only that "Biosimilar Manufacturers are

encouraged to consult publicly available data on expenditures for covered Part D drugs … which *may* allow them to determine the likelihood that a given drug *may* be a selected drug." CMS, Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026 ("Revised Guidance") at 109, 113 n.49 (June 30, 2023) (emphasis added). Yet the publicly available data is woefully outdated and insufficient to evaluate the potential for a given drug to be selected—as the Biosimilars Forum pointed out in comments it submitted to CMS to no avail.

The result is that under the IRA, especially as implemented by CMS, biosimilar manufacturers lack any visibility or clarity regarding which biological products CMS will select for the imposition of confiscatory, unconstitutional price controls. Manufacturers therefore have no way of determining whether they should invest in developing a biosimilar version of a particular reference product, or even whether or when they should submit a delay request under the Special Rule. The IRA's price-control scheme will also reduce the incentive for drug manufacturers to develop new, innovative products in the first place (especially for diseases that impact patients who are over age 65 and are thus primarily served by Medicare), which will in turn reduce the number of reference products available for biosimilar manufacturers to compete with.

III. CMS's extreme, one-sided, and purportedly unreviewable "guidance" exacerbates the harm to biosimilars and illustrates the constitutional problems with the IRA.

As explained above, Congress did not intend the IRA's price-control regime to replace the market-based check on biological product prices that is provided by competition from biosimilars under the BPCIA. On the contrary, Congress directed CMS *not* to impose price controls on any biological product for which a biosimilar version currently exists or is likely to come to market within two years.

At the same time, however, and consistent with the IRA's overall approach of delegating unchecked authority to CMS, the statute sought to shield CMS's implementation of these provisions from both public input and judicial scrutiny. The agency is directed to implement the IRA through "program instruction or other forms of program guidance," 42 U.S.C. §§ 1320f note, 1320f-1 note, which CMS interprets to mean that implementation is "not subject to the notice-and-comment requirement of the Administrative Procedure Act or the Medicare statute." CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments ("Initial Guidance") at 2 (Mar. 15, 2023). And on the back end, the IRA purports to bar "administrative or judicial review" of key aspects of the agency's implementation, including provisions governing the selection of drugs (including biological products) that will be subject to price controls and provisions concerning the Special Rule. *See* 42 U.S.C. § 1320f-7(2)-(3).

As plaintiffs' motion explains, these provisions violate the separation of powers and deny regulated entities due process by encouraging CMS to effectively rewrite the statute through unreviewable guidance. Unsurprisingly, CMS has taken an aggressive approach in wielding this purportedly unreviewable regulatory power. And in doing so, it has adopted a number of positions that contravene the statutory scheme, strip clarity and predictability from biosimilars manufacturers, and create an unworkable paradigm for biosimilar development. CMS's actions confirm that the prospect of agency overreach invited by the IRA's unconstitutional delegation scheme is not just theoretical—it is already happening.

For example, in an effort to sweep more reference biological products into the IRA's price-control regime (and thus squeeze out more biosimilars), CMS has adopted a novel, atextual interpretation of what it means for a biosimilar to be "marketed." As explained above, the IRA

provides that when a biosimilar is licensed and marketed (or during a period of special rule delay), CMS cannot impose price controls on the reference product for that biosimilar. *See* 42 U.S.C. § 1320f-1(c)(1), (e)(1)(B), (f)(1)(A). The term "marketed" has a well-understood meaning in the context of drugs and biological products—it refers to the introduction or delivery for introduction of a product into interstate commerce. *See, e.g.*, 21 C.F.R. § 314.3 (defining "commercial marketing" for generic drugs as "introduction or delivery for introduction into interstate commerce"). Indeed, CMS acknowledged this established meaning in its Initial Guidance under the IRA, where it defined "marketing" as "introduction or delivery for introduction into interstate commerce." Initial Guidance at 82.

Notwithstanding this established meaning, CMS announced that it will not consider a biosimilar to be "marketed"—even one that has been introduced into interstate commerce—unless, after considering the "totality of the circumstances," CMS deems the marketing of the biosimilar to be "bona fide" and conducive to what CMS considers "meaningful" competition. Revised Guidance at 2, 74. Seeking to maximize its own discretion, CMS stated that it "will review multiple data sources … holistically" to determine if a biosimilar manufacturer's marketing efforts measure up to CMS's ill-defined standard. *Id.* at 75.[7]

CMS's discretion-maximizing approach undermines the statutory scheme and translates into yet more potentially crippling uncertainty for the biosimilars industry. Under CMS's approach, a biosimilar manufacturer is deprived of even the meager certainty that any licensed biosimilar it is able to develop and launch will at least not be shut out of the market by reference

[7] CMS's approach means that a biosimilar may be faced with two inconsistent dates on which it is considered "marketed"—one for purposes of the IRA and a different one for purposes of the biosimilar pathway. *See* 42 U.S.C. § 262(k)(6)(A) (calculating the duration of first interchangeable exclusivity from "first commercial marketing"); *id.* § 262(*l*)(8)(A) (requiring notice of "first commercial marketing").

product prices artificially deflated by the IRA's price-control mechanism. Notwithstanding the *actual* date of marketing (when the biosimilar is introduced or delivered for introduction into interstate commerce), it may take weeks, months, or even longer before the biosimilar passes CMS's arbitrary threshold of "bona fide" marketing and "meaningful" competition. Myriad factors outside of a biosimilar manufacturer's control, from supply disruptions to physician education to the absence of midyear formulary changes, can affect the pace of biosimilar uptake. CMS's approach thus may lead to the imposition of price controls on a reference product despite the presence of biosimilar competition—and with no notice or due process for the affected biosimilar manufacturer. And biosimilar manufacturers will lack any certainty as to when, or even whether, they will be able to meet CMS's subjective standard. This uncertainty will substantially chill the incentives for companies to invest the resources and take the risks necessary to develop biosimilars.

CMS's approach is especially problematic for biosimilars that may come to market *after* CMS has already imposed price controls on the reference product. Under the IRA, reference product price controls are supposed to be removed once a biosimilar is licensed and "marketed." 42 U.S.C. § 1320f-1(c)(1). But so long as the reference product remains subject to price controls, it may be difficult, if not impossible, for a biosimilar to gain sufficient market share for CMS to deem the marketing "bona fide" and the resulting competition "meaningful." CMS's approach thus creates the prospect of a catch-22, where the reference product remains price-controlled because of insufficient competition and the competition is deemed insufficient because the reference product remains price-controlled.

CMS has also sought in numerous ways to limit the applicability of the IRA's "Special Rule." As explained above, the Special Rule provides for delaying the imposition of price controls

on biological products when there is a "high likelihood" that a biosimilar will be licensed and marketed within two years. 42 U.S.C. § 1320f-1(f). CMS's Guidance restricts the availability of the Special Rule by, among other things, requiring an applicant to demonstrate complete patent clearance, even though (unlike the norm for generic drugs) patent clearance is not necessary for biosimilar licensure or marketing. Specifically, the Guidance states that to establish a high likelihood of marketing within two years, a biosimilar manufacturer must demonstrate in its Special Rule application—which is due more than three months before the selected drugs list is even published—that either (1) there are no applicable non-expired patents relating to the reference product; (2) one or more court decisions establish that any potentially applicable patent is invalid, unenforceable, or not infringed by the biosimilar; or (3) the biosimilar manufacturer has signed an agreement with the reference-product manufacturer allowing it to market the biosimilar. Initial Guidance at 19; *see also* Revised Guidance at 24, 111-12.

CMS's requirement that a biosimilar manufacturer demonstrate complete patent clearance before the start of the two-year delay period is contrary to the IRA's plain text and undermines the scheme Congress created in the BPCIA. Nothing in the BPCIA precludes licensure or marketing of a biosimilar due to any ongoing or threatened patent litigation. In this respect, the BPCIA stands in sharp contrast to the rules applicable to non-biological generic drugs under the Food, Drug, and Cosmetic Act, which provides that a timely filed patent lawsuit by a reference listed drug manufacturer automatically stays FDA's approval of a generic drug for 30 months. *See* 21 U.S.C. § 355(j)(5)(B)(iii). The BPCIA includes no similar automatic-stay provision, meaning that FDA can approve a biosimilar application notwithstanding any initiated patent litigation, and a biosimilar is free to launch "at risk" (*i.e.*, subject to the risk of patent-infringement liability) at any point post-approval. A biosimilar manufacturer may thus have both robust evidence that a patent

asserted against it is invalid, unenforceable, or not infringed and definite plans to launch notwithstanding any ongoing patent litigation. Yet under CMS's standard, such a manufacturer cannot show a high likelihood of marketing within the statutory period. By assuming that a biosimilar cannot be marketed if there is any risk of or ongoing patent litigation, CMS disregards Congress's deliberate choice to permit biosimilar licensure regardless of any patent litigation between the biosimilar applicant and the reference product sponsor. And CMS issued its guidance regarding the Special Rule "as final … without public comment." Initial Guidance at 2.

These are just a few examples of the many ways in which CMS has sought to use unreviewable guidance to arrogate more power to itself under the IRA. In these ways and more, CMS's implementation of the IRA disregards the realities of the biosimilars industry and will harm patients by undermining the development of life-saving and life-improving biosimilar medicines.

These actions by CMS do not occur in a vacuum—they are the direct result of the IRA's unconstitutional scheme, which delegates unbounded authority to CMS with hardly any meaningful statutory limits, while simultaneously encouraging CMS to disregard the few limits that exist by purporting to insulate CMS's actions from both public input and administrative and judicial review. Under a constitutional statute, agency overreach like CMS's restrictive interpretation of "marketed" and its undue narrowing of the Special Rule would be checked by public input on the front end and administrative and judicial review on the back end. These guardrails are essential for a delegation of broad price-setting authority to an unelected agency to comport with the separation of powers, and they are also critical elements of due process. By eliminating those guardrails in the IRA, Congress overstepped constitutional bounds.

CONCLUSION

The Court should grant plaintiffs' motion for summary judgment.

Respectfully submitted,

/s/ J. Carl Cecere

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Dated: August 24, 2023

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CERTIFICATE OF SERVICE

I hereby certify that on August 24, 2023, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

/s/ J. Carl Cecere

J. Carl Cecere